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CENTRAL FAX CENTERApplication No. 09/523,776
Amendment dated June 24, 2008
Reply to Office Action dated December 27, 2007

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Docket No.: 49632(71699)

REMARKS

Claims 48, 51 and 55 are pending. Applicant makes these amendments without prejudice to pursuing the original subject matter of this application in a later filed application claiming benefit of the instant application, including without prejudice to any determination of equivalents of the claimed subject matter. Support for these amendments appears throughout the specification and claims as filed. No new matter is introduced by these amendments.

Rejection under 35 U.S.C. § 103(a)

Claims 48, 51 and 55 are rejected as unpatentable over Herron (US Patent 4,764,521) in view of Rubenstein (IDS, CJ) and Rephaeli et al. (US Patent 5,939,455). Applicant traverses.

Particularly in response to the section titled "Response to the Arguments" at page 4 of the Action, it is asserted in the Action that the previously submitted 132 declaration by Dr. Zeitlin and submission of a review article (Zeitlin, *N. Engl. J Med.* 351:6 pp. 606-608 (2004)) describing the role of the $\Delta F508$ allele in patients with cystic fibrosis ("CF") was not found to be persuasive to overcome the rejection based upon Herron in view of Rubenstein et al. and Rephaeli et al. or Faller. It is asserted that those evidences are still not sufficient to the establishment of a *prima facie* case of unexpected benefit. In particular, it is noted that (i) cinnamic acid is inferior to control; (ii) there is no evidence that the mechanism disclosed by Zeitlin is the only pathway for treatment of cystic fibrosis; and (iii) finally it is asserted in the Action that even were that pathway the solo pathway for treatment of cystic fibrosis, "that it is not a difficult matter to carry out a process in such a fashion that it will not be successful and, therefore the failures of experimenters who have no interest in succeeding should not be accorded great weight", seemingly implying that Dr. Zeitlin's experimental results lack appropriate scientific rigor at best, and at worst are unduly manipulated to further her personal goals. Applicant traverses and strongly objects to both the asserted analysis and

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intimations. Dr. Zeitlin's results are based on sound scientific protocol, and demonstrate that trans-SAA has superior function to both 4-PBA and cinnamic acid.

First, Applicant reiterates their disagreement with the assertion that Rephaeli teaches 4-PBA or cinnamic acid for treatment of cystic fibrosis. This assertion is premised on a combination of two broadbrush stroke interpretations of two passages: (1) col. 1, lines 15-29 (stating that broad classes of compounds, i.e., oxyalkylene-containing compounds, butyric acid, butyric acid salts, and butyric acid derivatives) are useful for treating any of 14 broad classes of diseases (e.g., cancer, cutaneous ulcers, gastrointestinal disorders, blood disorders, immunomodulation, etc.); and (2) col. 10, lines 18-22, listing 11 compounds as butyric acid derivatives. Applicant disagrees with an assertion that Rephaeli provides a teaching of which compounds are useful against which disease indications with a reasonable expectation of success. Moreover, Rubenstein fails to teach unsaturated, 4-carbon chain compounds, and (as stated in the Action) Herron does not teach unsubstituted caryl carboxylic acid compounds. As such, Applicant traverses as a matter of course that a *prima* case of obviousness is established in the Action.

Nonetheless, it is well established that the presence of an unexpected property is evidence of nonobviousness. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (where a claimed compound that was structurally similar to a prior art compound was found nonobvious because it possessed properties not possessed by the prior art compound). It is also well established that superiority of a property shared with the prior art is evidence of nonobviousness. *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Here, the claimed compound, trans-SAA, is demonstrated (as stated in the declaration filed March 5, 2007 in the instant application) to have at least superior activity and/or the presence of an unexpected property over art compounds 4-PBA and cinnamic acid in regard to promotion of trafficking of functional $\Delta F508$ -CFTR to the cell surface (which as discussed in detail below, is highly relevant to therapeutic treatment of CF).

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In the Action, it is overlooked that the results establish just that, i.e., that trans-SAA is a superior compound for promotion of trafficking of functional $\Delta F508$ -CFTR to the cell surface. Nowhere has Applicant intimated that cinnamic acid is "inactive" as stated in the Action, nor has Applicant made any assertion of inoperability of any reference, including Rephaeli. Although as discussed above, Applicant disagrees that the cited passages of Rephaeli in fact teach cinnamic acid for treatment of cystic fibrosis; regardless, the point is that trans-SAA possesses demonstrated superior activity in promotion of trafficking of functional $\Delta F508$ -CFTR to the cell surface over art compounds 4-PBA and cinnamic acid. See, previously submitted Zeitlin Declaration. Furthermore, Applicant submits a second declaration of Dr. Pamela Zeitlin herewith, stating that it is her expert opinion and established in the art that the mutation involving deletion of a phenylalanine residue at position 508 ($\Delta F508$ -CFTR) is a very significant (i.e., 70% of patient population), if not primary, mechanism of CF etiology; thus making control of such trafficking a relevant treatment protocol for a majority of CF patients. As such, the promotion of $\Delta F508$ -CFTR trafficking by trans-SAA is a property that is both relevant and surprisingly unexpected. Applicants submit that this showing more than establishes sufficient evidence to rebut the rejection.

Based on the foregoing, Applicant respectfully submits that the rejection is overcome and requests withdrawal of the rejection.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. Should any of the claims not be found to be in condition for allowance, the Examiner is requested to call Applicants' undersigned representative to discuss the application. Applicants thank the Examiner in advance for this courtesy.

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The Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 49632(71699).

Dated: June 24, 2008

Respectfully submitted,

By

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